

1 WHAT IS CLAIMED IS:

1 1. A transgenic knockout mouse whose genome comprises a disruption in
2 the mouse's endogenous melanopsin gene, wherein the disruption prevents the expression of a
3 functional melanopsin protein in cells of the mouse.

1 2. The transgenic knockout mouse of claim 1, wherein the mouse
2 comprises a homozygous disruption of the melanopsin gene.

1 3. The method of claim 1, the homozygous disruption results in the
2 transgenic knockout mouse exhibiting an attenuated circadian rhythm phase-shift in response
3 to a light pulse during a dark portion of an environmental dark/light cycle.

1 4. A cell isolated from the transgenic knockout mouse of claim 1,
2 wherein the genome of the cell comprises a disruption in its endogenous melanopsin gene,
3 and wherein the homozygous disruption prevents the expression of a functional melanopsin
4 protein in said cell.

1 5. A method for identifying a therapeutic agent for modulating circadian
2 rhythm in a mammal, the method comprising:

3 administering an agent to a transgenic knockout animal whose genome
4 comprises a disruption in its endogenous melanopsin gene, wherein the disruption prevents
5 the expression of a functional melanopsin protein in cells of the animal and the animal
6 comprises a homozygous disruption of the melanopsin gene; and

7 selecting an agent that modulates the regulation of circadian rhythm in the
8 animal.

1 6. The method of claim 5, wherein the knockout animal displays an
2 attenuated circadian rhythm phase-shift response to a light pulse during a dark portion of an
3 environmental dark/light cycle.

1 7. The method of claim 5, wherein the selecting step comprises selecting
2 an agent that enhances the animal's circadian rhythm phase-shift response to a light pulse
3 during a dark portion of an environmental dark/light cycle.

1 8. The method of claim 5, wherein the animal is a mouse.

1 9. A method of modulating circadian rhythm in a mammal in need
2 thereof, the method comprising administering to the mammal an effective amount of the
3 agent selected in claim 5.

1 10. The method of claim 9, wherein timing of administration of the
2 selected agent is pre-determined to coincide with an appropriate phase of an existing
3 circadian rhythm to produce a selected modulation of the circadian rhythm.

1 11. The method of claim 9, wherein the selected agent is used to treat or
2 prevent a sleep disorder.

1 12. The method of claim 9, wherein the mammal has a condition selected
2 from the group selected from insomnia, Seasonal Affective Disorder, Shift Work
3 dysrhythmia, delayed-sleep phase syndrome, and jet-lag.

1 13. The method of claim 9, wherein the mammal is a human.

1 14. The method of claim 9, wherein the selected agent is administered in
2 conjunction with melatonin or a compound that suppresses or stimulates melatonin
3 production.

1 15. The method of claim 9, wherein the selected agent is administered in
2 conjunction with light therapy.

1 16. A method of modulating circadian rhythm in a mammal in need
2 thereof, the method comprising administering to the mammal an effective amount of a
3 melanopsin modulator.

1 17. The method of claim 16, wherein timing of administration of the
2 modulator is pre-determined to coincide with an appropriate phase of an existing circadian
3 rhythm to produce a selected modulation of the circadian rhythm.

1 18. The method of claim 16, wherein the modulator is used to treat or
2 prevent a sleep disorder.

1 19. The method of claim 16, wherein the mammal has a condition selected
2 from the group selected from insomnia, Seasonal Affective Disorder, Shift Work
3 dysrhythmia, delayed-sleep phase syndrome, and jet-lag.

1 20. The method of claim 16, wherein the mammal is a human.

1 21. The method of claim 16, wherein the modulator is administered in
2 conjunction with melatonin or a compound that suppresses or stimulates melatonin
3 production.